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L5: Entry 1 of 2

File: USPT

Feb 4, 2003

DOCUMENT-IDENTIFIER: US 6515018 B1

TITLE: Synergistic compositions for lycopene and Vitamin E for the prevention of LDL oxidation

Other Reference Publication (4):

Stahl et al., "Carotenoid mixtures protect multilamellar liposomes against oxidative damage: synergistic effects of lycopene and lutein", FEBS Letters, vol. 427, No. 2, pp. 305-308, (1998).

WEST[Generate Collection](#)[Print](#)**Search Results - Record(s) 1 through 29 returned.**☐ 1. Document ID: US 6515018 B1

L1: Entry 1 of 29

File: USPT

Feb 4, 2003

US-PAT-NO: 6515018

DOCUMENT-IDENTIFIER: US 6515018 B1

TITLE: Synergistic compositions for lycopene and Vitamin E for the prevention of LDL oxidation

DATE-ISSUED: February 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Fuhrman; Bianca	Haifa			IL
Aviram; Michael	Kiryat Haim			IL
Nir; Zohar	Meitar			IL
Zelkha; Morris	Omer			IL

US-CL-CURRENT: 514/458; 424/727

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC
Draw Desc	Image										

☐ 2. Document ID: US 6428816 B1

L1: Entry 2 of 29

File: USPT

Aug 6, 2002

US-PAT-NO: 6428816

DOCUMENT-IDENTIFIER: US 6428816 B1

TITLE: Carotenoid agent for inhibiting the conversion of epithelial cells to tumors

DATE-ISSUED: August 6, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schlipalius; Lance Elliot	Ashwood			AU
Buckmeier; Julie A.	Long Beach	CA		
Meyskens, Jr.; Frank L.	Irvine	CA		

US-CL-CURRENT: 424/725; 424/773, 514/725, 514/938

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC
Draw Desc	Image										

☐ 3. Document ID: US 6384090 B2

L1: Entry 3 of 29

File: USPT

May 7, 2002

US-PAT-NO: 6384090

DOCUMENT-IDENTIFIER: US 6384090 B2

TITLE: Preparation of active ingredient dispersions and apparatus therefor

DATE-ISSUED: May 7, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Riede; Thomas	Bensheim			DE
Gobel; Werner	Meckenheim			DE
Lockemann; Christian	Mannheim			DE

US-CL-CURRENT: 516/31; 422/255, 422/281, 424/450, 504/362, 514/725, 516/9, 516/926

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMIC
Draw Desc	Image										

☐ 4. Document ID: US 6375873 B1

L1: Entry 4 of 29

File: USPT

Apr 23, 2002

US-PAT-NO: 6375873

DOCUMENT-IDENTIFIER: US 6375873 B1

TITLE: Process and apparatus for producing stably fine-particle powders

DATE-ISSUED: April 23, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lockemann; Christian	Mannheim			DE
Luddecke; Erik	Mutterstadt			DE
Horn; Dieter	Heidelberg			DE

US-CL-CURRENT: 264/7; 264/13, 264/5, 425/6

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 5. Document ID: US 6312703 B1

L1: Entry 5 of 29

File: USPT

Nov 6, 2001

US-PAT-NO: 6312703

DOCUMENT-IDENTIFIER: US 6312703 B1

TITLE: Compressed lecithin preparations

DATE-ISSUED: November 6, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Orthoefer; Frank T.	Chesterfield	MO		

US-CL-CURRENT: 424/401; 424/400, 424/450, 424/59, 424/65, 514/78, 514/844

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMC
Draw Desc	Image									

☐ 6. Document ID: US 6258855 B1

L1: Entry 6 of 29

File: USPT

Jul 10, 2001

US-PAT-NO: 6258855

DOCUMENT-IDENTIFIER: US 6258855 B1

TITLE: Method of retarding and ameliorating carpal tunnel syndrome

DATE-ISSUED: July 10, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lorenz; R. Todd	Kailua-Kona	HI		
Cysewski; Gerald R.	Kailua-Kona	HI		

US-CL-CURRENT: 514/691

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMC
Draw Desc	Image									

☐ 7. Document ID: US 6218599 B1

L1: Entry 7 of 29

File: USPT

Apr 17, 2001

US-PAT-NO: 6218599

DOCUMENT-IDENTIFIER: US 6218599 B1

TITLE: Polynucleotide molecule from Haematococcus pluvialis encoding a polypeptide having a .beta.-C-4-oxygenase activity for biotechnological production of (3S, 3'S) astaxanthin and its specific expression in chromoplasts of higher plants

DATE-ISSUED: April 17, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hirschberg; Joseph	Jerusalem			IL
Lotan; Tamar	Kineret			IL

US-CL-CURRENT: 800/295; 435/189, 435/252.3, 435/252.33, 435/254.11, 435/320.1, 435/410, 536/23.1, 536/23.2, 536/23.74, 800/298

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KMIC

☐ 8. Document ID: US 6200597 B1

L1: Entry 8 of 29

File: USPT

Mar 13, 2001

US-PAT-NO: 6200597

DOCUMENT-IDENTIFIER: US 6200597 B1

**** See image for Certificate of Correction ****

TITLE: Formulation and use of carotenoids in treatment of cancer

DATE-ISSUED: March 13, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mehta; Kapil	Houston	TX		
Perez-Soler; Roman	Houston	TX		
Lopez-Berestein; Gabriel	Houston	TX		
Lenk; Robert	Willis	TX		
Hayman; Alan C.	late of The Woodlands	TX		

US-CL-CURRENT: 424/450; 514/725

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KMIC

☐ 9. Document ID: US 6197836 B1

L1: Entry 9 of 29

File: USPT

Mar 6, 2001

US-PAT-NO: 6197836

DOCUMENT-IDENTIFIER: US 6197836 B1

TITLE: Preparation of active ingredient dispersions and apparatus therefor

DATE-ISSUED: March 6, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Riede; Thomas	Beuschieriez			DE
Gobel; Werner	Meckenheim			DE
Lockemann; Christian	Mannheim			DE

US-CL-CURRENT: 516/31; 422/255, 514/725, 516/9, 516/926

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KMIC

☐ 10. Document ID: US 6083529 A

L1: Entry 10 of 29

File: USPT

Jul 4, 2000

US-PAT-NO: 6083529

DOCUMENT-IDENTIFIER: US 6083529 A

TITLE: Liposome encapsulated active agent dry powder composition

DATE-ISSUED: July 4, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Manzo; Robert P.	Goshen	NY		
Vollhardt; Jurgen	Holzminden			DE
Malkan; Nisha	Nanuet	NY		
Friars; Gary	Midland Park	NJ		

US-CL-CURRENT: 424/450; 424/484, 424/485, 424/488, 424/489, 424/490, 424/493,
424/496, 424/499, 424/500, 424/69

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 11. Document ID: US 5965795 A

L1: Entry 11 of 29

File: USPT

Oct 12, 1999

US-PAT-NO: 5965795

DOCUMENT-IDENTIFIER: US 5965795 A

TITLE: Polynucleotide molecule from Haematococcus pluvialis encoding a polypeptide having a beta-C-4-oxygenase activity for biotechnological production of (3S, 3'S) astaxanthin and its specific expression in chromoplasts of higher plants

DATE-ISSUED: October 12, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hirschberg; Joseph	Jerusalem			IL
Lotan; Tamar	Kineret			IL

US-CL-CURRENT: 800/295; 435/183, 435/189, 435/252.3, 435/252.33, 435/254.11,
435/254.21, 435/320.1, 435/410, 536/23.1, 536/23.2, 536/23.74

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 12. Document ID: US 5916791 A

L1: Entry 12 of 29

File: USPT

Jun 29, 1999

US-PAT-NO: 5916791

DOCUMENT-IDENTIFIER: US 5916791 A

TITLE: Polynucleotide molecule from Haematococcus pluvialis encoding a polypeptide

having a .beta.--C--4--oxygenase activity for biotechnological production of (3S,3S)astaxanthin

DATE-ISSUED: June 29, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hirschberg; Joseph	93714 Jerusalem			IL
Lotan; Tamar	Moshava			IL

US-CL-CURRENT: 435/189; 435/183, 435/252.3, 435/252.33, 435/325, 435/410, 435/423, 536/23.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
Draw Desc	Image									

☐ 13. Document ID: US 5906811 A

L1: Entry 13 of 29

File: USPT

May 25, 1999

US-PAT-NO: 5906811

DOCUMENT-IDENTIFIER: US 5906811 A

TITLE: Intra-oral antioxidant preparations

DATE-ISSUED: May 25, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Herish; Theodore	Atlanta	GA		

US-CL-CURRENT: 424/54; 424/49, 604/58

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
Draw Desc	Image									

☐ 14. Document ID: US 5897871 A

L1: Entry 14 of 29

File: USPT

Apr 27, 1999

US-PAT-NO: 5897871

DOCUMENT-IDENTIFIER: US 5897871 A

TITLE: Therapeutic agent for the treatment of melanomas

DATE-ISSUED: April 27, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schlipalius; Lance Elliott	Ashwood			AU

US-CL-CURRENT: 424/423

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KIMC

☐ 15. Document ID: US 5827886 A

L1: Entry 15 of 29

File: USPT

Oct 27, 1998

US-PAT-NO: 5827886

DOCUMENT-IDENTIFIER: US 5827886 A

TITLE: Composition for relief of arthritis-induced symptoms

DATE-ISSUED: October 27, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Heresh; Theodore	Atlanta	GA		

US-CL-CURRENT: 514/562; 424/702, 514/162, 514/165, 514/171, 514/474, 514/561, 514/627

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KIMC

☐ 16. Document ID: US 5811119 A

L1: Entry 16 of 29

File: USPT

Sep 22, 1998

US-PAT-NO: 5811119

DOCUMENT-IDENTIFIER: US 5811119 A

**** See image for Certificate of Correction ****

TITLE: Formulation and use of carotenoids in treatment of cancer

DATE-ISSUED: September 22, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mehta; Kapil	Houston	TX		
Perez-Soler; Roman	Houston	TX		
Lopez-Berestein; Gabriel	Houston	TX		
Lenk; Robert P.	Willis	TX		
Hayman, deceased; Alan C.	late of Houston	TX		

US-CL-CURRENT: 424/450

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KIMC

☐ 17. Document ID: US 5783211 A

L1: Entry 17 of 29

File: USPT

Jul 21, 1998

US-PAT-NO: 5783211

DOCUMENT-IDENTIFIER: US 5783211 A

TITLE: Liposome encapsulated active agent dry powder composition

DATE-ISSUED: July 21, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Manzo; Robert P.	Goshen	NY		
Vollhardt; Jurgen	Bevern	NY		
Malkan; Nisha	Nanuet	NY		
Friars; Gary	Midland Park	NJ		

US-CL-CURRENT: [424/450](#); [424/484](#), [424/485](#), [424/488](#), [424/489](#), [424/490](#), [424/493](#),
[424/496](#), [424/499](#), [424/500](#), [424/69](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMC
Draw Desc	Image									

☐ 18. Document ID: US 5773026 A

L1: Entry 18 of 29

File: USPT

Jun 30, 1998

US-PAT-NO: 5773026

DOCUMENT-IDENTIFIER: US 5773026 A

TITLE: Aqueous formulations of water-insoluble therapeutic agent comprising carotenoids and/or tocopherols

DATE-ISSUED: June 30, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schlipalius; Lance Elliott	Ashwood			AU

US-CL-CURRENT: [424/450](#); [424/531](#), [424/78.02](#), [514/937](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMC
Draw Desc	Image									

☐ 19. Document ID: US 5705180 A

L1: Entry 19 of 29

File: USPT

Jan 6, 1998

US-PAT-NO: 5705180

DOCUMENT-IDENTIFIER: US 5705180 A

TITLE: Therapeutic agent for the treatment of melanomas

DATE-ISSUED: January 6, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schlipalius; Lance Elliott	Ashwood			AU

US-CL-CURRENT: 424/423

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 20. Document ID: US 5554374 A

L1: Entry 20 of 29

File: USPT

Sep 10, 1996

US-PAT-NO: 5554374

DOCUMENT-IDENTIFIER: US 5554374 A

TITLE: Skin preparation using nanospheres

DATE-ISSUED: September 10, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Olivier-Terras; Josette	Peronnas			FR

US-CL-CURRENT: 424/401; 424/450, 424/491, 424/59, 424/60, 514/844

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 21. Document ID: US 5034228 A

L1: Entry 21 of 29

File: USPT

Jul 23, 1991

US-PAT-NO: 5034228

DOCUMENT-IDENTIFIER: US 5034228 A

**** See image for Certificate of Correction ****TITLE: Pharmaceutical composition, in particular dermatological or cosmetic, comprising hydrous lipidic lamellar phases or liposomes containing a retinoid or a structural analogue thereof such as a carotenoid

DATE-ISSUED: July 23, 1991

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Meybeck; Alain	Courbevoie			FR
Michelon; Philippe	Paris			FR
Montastier; Christiane	Maisons-Lafitte			FR
Redziniak; Gerard	Saint-Cyr-En-Val			FR

US-CL-CURRENT: 424/401; 424/450, 436/829, 514/859

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 22. Document ID: JP 2001002566 A

L1: Entry 22 of 29

File: JPAB

Jan 9, 2001

PUB-NO: JP02001002566A
DOCUMENT-IDENTIFIER: JP 2001002566 A
TITLE: STABILIZED LIPOSOME AND ITS FORMATION

PUBN-DATE: January 9, 2001

INVENTOR-INFORMATION:

NAME

COUNTRY

HARA, MASAYUKI

MIYAKE, ATSUSHI

HOSHINO, TAKAYUKI

YOKOYAMA, AKIHIRO

INT-CL (IPC): A61 K 9/127; A61 K 47/22; A61 K 47/24

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KIMC

☐ 23. Document ID: WO 2064110 A2

L1: Entry 23 of 29

File: EPAB

Aug 22, 2002

PUB-NO: WO002064110A2
DOCUMENT-IDENTIFIER: WO 2064110 A2
TITLE: CAROTENOID-LOADED LIPOSOMES

PUBN-DATE: August 22, 2002

INVENTOR-INFORMATION:

NAME

COUNTRY

BARENHOLZ, YECHEZKEL

IL

DIMINSKY, DVORAH

IL

COHEN, RIVKA

IL

INT-CL (IPC): A61 K 9/00
EUR-CL (EPC): A61K009/127; A61K008/14, A61K008/31 , A61Q017/00 , A61Q017/04 ,
A61Q019/00

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KIMC

☐ 24. Document ID: WO 9604891 A1

L1: Entry 24 of 29

File: EPAB

Feb 22, 1996

PUB-NO: WO009604891A1
DOCUMENT-IDENTIFIER: WO 9604891 A1

TITLE: FORMULATION AND USE OF CAROTENOIDS IN TREATMENT OF CANCER

PUBN-DATE: February 22, 1996

INVENTOR-INFORMATION:

NAME	COUNTRY
MEHTA, KAPIL	
PEREZ-SOLER, ROMAN	
LOPEZ-BERESTEIN, GABRIEL	
LENK, ROBERT P	
HAYMAN, ALAN C	

INT-CL (IPC): A61 K 9/127

EUR-CL (EPC): A61K031/203; A61K009/127

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KIMC
Draw Desc	Image									

☐ 25. Document ID: WO 9313751 A1

L1: Entry 25 of 29

File: EPAB

Jul 22, 1993

PUB-NO: WO009313751A1

DOCUMENT-IDENTIFIER: WO 9313751 A1

TITLE: FORMULATION AND USE OF CAROTENOIDS IN TREATMENT OF CANCER

PUBN-DATE: July 22, 1993

INVENTOR-INFORMATION:

NAME	COUNTRY
MEHTA, KAPIL	US
PEREZ-SOLER, ROMAN	US
LOPEZ-BERESTEIN, GABRIEL	US
LENK, ROBERT P	US
HAYMAN, ALAN C	US

US-CL-CURRENT: 280/21.1; 280/22.1

INT-CL (IPC): A61K 9/127; A61K 31/20

EUR-CL (EPC): A61K031/203; A61K009/127, A61K031/20

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KIMC
Draw Desc	Image									

☐ 26. Document ID: US 20030059462 A1 WO 200264110 A2

L1: Entry 26 of 29

File: DWPI

Mar 27, 2003

DERWENT-ACC-NO: 2002-599922

DERWENT-WEEK: 200325

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TITLE: Formulation used for treating diseases caused by singlet oxygen e.g. cancer and cardiovascular disorders comprises liposomes loaded with carotenoid immiscible in water

INVENTOR: BARENHOLZ, Y; COHEN, R ; DIMINSKY, D

PRIORITY-DATA: 2001US-268185P (February 13, 2001), 2002US-0073365 (February 13, 2002)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 20030059462 A1	March 27, 2003		000	A61K009/127
WO 200264110 A2	August 22, 2002	E	040	A61K009/00

INT-CL (IPC): A61 K 9/00; A61 K 9/127; A61 K 31/01; A61 K 31/12

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMC
Draw Desc	Image									

☐ 27. Document ID: JP 2001002566 A JP 3138733 B2

L1: Entry 27 of 29

File: DWPI

Jan 9, 2001

DERWENT-ACC-NO: 2001-293982

DERWENT-WEEK: 200131

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TITLE: Stable liposome as carrier for use in drug delivery systems, contains phosphatidylcholine containing liposome film stabilized by carotenoid film modified with sugar moiety

PRIORITY-DATA: 1999JP-0177486 (June 23, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 2001002566 A	January 9, 2001		008	A61K009/127
JP 3138733 B2	February 26, 2001		007	A61K009/127

INT-CL (IPC): A61 K 9/127; A61 K 47/22; A61 K 47/24; A61 K 47/26

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMC
Draw Desc	Image									

☐ 28. Document ID: EP 1016454 A1 US 6375873 B1 DE 19860497 A1 JP 2000225333 A CN 1264614 A

L1: Entry 28 of 29

File: DWPI

Jul 5, 2000

DERWENT-ACC-NO: 2000-433175

DERWENT-WEEK: 200232

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TITLE: Preparation of stable fine particle powders comprising active agent and excipient, by separately dissolving in super-critical, compressible fluid, then relaxing fluid

INVENTOR: HORN, D; LOCKEMANN, C ; LUEDDECKE, E

PRIORITY-DATA: 1998DE-1060497 (December 28, 1998)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 1016454 A1	July 5, 2000	G	010	B01J002/00
US 6375873 B1	April 23, 2002		000	B29B009/10
DE 19860497 A1	July 6, 2000		000	B01J003/00
JP 2000225333 A	August 15, 2000		023	B01J019/00
CN 1264614 A	August 30, 2000		000	B01J002/00

INT-CL (IPC): A61 J 3/02; B01 J 2/00; B01 J 2/04; B01 J 3/00; B01 J 13/06; B01 J 19/00; B29 B 9/10

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KIMC
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☐ 29. Document ID: EP 229561 A JP 2855105 B2 FR 2591105 A JP 62215513 A ES 2003605 A US 5034228 A CA 1298195 C EP 229561 B1 DE 3686325 G JP 93015689 B JP 09110669 A

L1: Entry 29 of 29

File: DWPI

Jul 22, 1987

DERWENT-ACC-NO: 1987-200045

DERWENT-WEEK: 199911

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TITLE: Pharmaceutical or cosmetic compsns. contg. retinoid cpds. - encapsulated in liposome(s) which reduces skin irritant effects

INVENTOR: MEYBECK, A; MICHELON, P ; MONTASTIER, C ; REDZINIAK, G

PRIORITY-DATA: 1985FR-0018362 (December 11, 1985)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 229561 A	July 22, 1987	F	019	
JP 2855105 B2	February 10, 1999		003	A61K007/00
FR 2591105 A	June 12, 1987		000	
JP 62215513 A	September 22, 1987		000	
ES 2003605 A	November 1, 1988		000	
US 5034228 A	July 23, 1991		008	
CA 1298195 C	March 31, 1992		000	
EP 229561 B1	August 5, 1992	F	021	A61K009/50
DE 3686325 G	September 10, 1992		000	A61K009/50
JP 93015689 B	March 2, 1993		010	A61K007/48
JP 09110669 A	April 28, 1997		009	A61K007/48

INT-CL (IPC): A61K 7/00; A61K 7/06; A61K 7/42; A61K 7/48; A61K 9/127; A61K 9/50; A61K 31/015; A61K 31/07; A61K 37/22

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KIMC
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carotenoid\$ same liposome\$	29

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L5: Entry 1 of 2

File: USPT

Feb 4, 2003

US-PAT-NO: 6515018

DOCUMENT-IDENTIFIER: US 6515018 B1

TITLE: Synergistic compositions for lycopene and Vitamin E for the prevention of LDL oxidation

DATE-ISSUED: February 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Fuhrman; Bianca	Haifa			IL
Aviram; Michael	Kiryat Haim			IL
Nir; Zohar	Meitar			IL
Zelkha; Morris	Omer			IL

US-CL-CURRENT: [514/458](#); [424/727](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC
Draw Desc	Image										

☐ 2. Document ID: US 20030059462 A1 WO 200264110 A2

L5: Entry 2 of 2

File: DWPI

Mar 27, 2003

DERWENT-ACC-NO: 2002-599922

DERWENT-WEEK: 200325

COPYRIGHT 2003 DERWENT INFORMATION LTD

TITLE: Formulation used for treating diseases caused by singlet oxygen e.g. cancer and cardiovascular disorders comprises liposomes loaded with carotenoid immiscible in water

INVENTOR: BARENHOLZ, Y; COHEN, R ; DIMINSKY, D

PRIORITY-DATA: 2001US-268185P (February 13, 2001), 2002US-0073365 (February 13, 2002)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 20030059462 A1	March 27, 2003		000	A61K009/127
WO 200264110 A2	August 22, 2002	E	040	A61K009/00

INT-CL (IPC): [A61 K 9/00](#); [A61 K 9/127](#); [A61 K 31/01](#); [A61 K 31/12](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KM/C
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Terms	Documents
lycopene same liposome\$	2

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L6: Entry 4 of 39

File: USPT

Apr 30, 2002

DOCUMENT-IDENTIFIER: US 6379697 B1

TITLE: Stabilization of photosensitive materials

Detailed Description Text (29):

Riboflavin gamma-cyclodextrin inclusion complexes were entrapped in DRV incorporating a light absorbing agent or antioxidant in their lipid phase selected from: oil Red O, oxybenzone, deoxybenzone and beta-carotene or combinations thereof. The resulting liposomes were exposed to UV light (254/365 nm) and their photodegradation at different time intervals monitored spectrophotometrically (excitation 445 nm, emission 520 nm). As in the previous examples this degradation followed first order kinetics represented by the equations given earlier.

Detailed Description Text (30):

The results obtained, shown graphically in FIG. 2, indicate that the photostability of riboflavin entrapped alone in DRV increases 4-fold (line 2) compared to that for free riboflavin in water (line 1). A modest increase in photostability (to 6-fold) is also obtained with riboflavin-gamma-cyclodextrin inclusion complex in water (line 3). Stability is increased 20-fold when riboflavin-gamma-cyclodextrin inclusion complex is entrapped in DRV (line 4) and 210-fold when co-entrapped in DRV with oil Red O, oxybenzone and deoxybenzone (line 5). Stability values reach a maximum (260-fold increase) when the anti-oxidant beta-carotene is included in the liposomes containing the riboflavin-gamma-cyclodextrin inclusion complex and the light absorbing agents (line 6).

Detailed Description Text (68):

The incorporation of the antioxidant betacarotene with several lipid soluble light absorbers further increased the photostability of the vitamin. It is thought that the antioxidant was responsible for inhibiting UV radical mediated photoresponse as well as protecting the lipids of the liposome from oxidation.

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L6: Entry 24 of 39

File: USPT

Jun 30, 1998

DOCUMENT-IDENTIFIER: US 5773026 A

TITLE: Aqueous formulations of water-insoluble therapeutic agent comprising carotenoids and/or tocopherols

Brief Summary Text (11):

To date several in vitro studies have taken place to determine the effect of beta-carotene on normal and transformed cell types using solvents to solubilise the beta-carotene such as tetrahydrofuran, butanol, chloroform, hexane, dimethylsulfoxide, ethanol or in a liposome micelle. Previous liposome preparations have shown toxicity in cell line cultures as well as being limited in application. (see Bertram J.S., Pung A, Churley M., et al: Diverse carotenoids protect against chemically induced neoplastic transformation. Carcinogenesis 12:671-678, 1991; Hazuka M.B., Prasad-Edwards J., Newman F., et al: Beta-carotene induces morphological differentiation and decreases adenylate cyclase activity in melanoma cells in culture. J Am Coll Nutr 9:143-149, 1990; Schultz T.D., Chew B.P., Seaman W.R., et al: Inhibitory effect of conjugated dienolic derivatives of linoleic acid and beta-carotene on the in vitro growth of human cancer cells. Canc Letters 63:125-133, 1992; Schwartz J.L., Shklar G.: The selective cytotoxic effect of carotenoids and a-tocopherol on human cancer cell lines in vitro. J Oral Maxillofac Surg 50:367-373, 1992; Schwartz J.L., Tanaka J., Khandekar V., et al: Beta-Carotene and/or Vitamin E as modulators of alkylating agents in SCC-25 human squamous carcinoma cells. Canc Chemother Pharmacol 29:207-213, 1992; Zhang L-X, Cooney R.V., Bertram J.S.: Carotenoids enhance gap junctional communication and inhibit lipid peroxidation in C3H/10T1/2 cells: relationship to their cancer chemopreventive action. Carcinogenesis 12:2109-2114, 1991; and Zhang L-X, Cooney R.V., Bertram J.S.: Carotenoids up-regulate connexin 43 gene expression independent of their provitamin A or antioxidant properties. Canc Res 52:5707-5712, 1992). However, these solvents have been found to have a toxic effect which is dose dependent. These solvents are also incompatible with human blood or lymph for the purposes of intravenous or injectable preparations.

WEST[Generate Collection](#)[Print](#)**Search Results - Record(s) 1 through 30 of 39 returned.**☐ 1. Document ID: US 6485950 B1

L6: Entry 1 of 39

File: USPT

Nov 26, 2002

US-PAT-NO: 6485950

DOCUMENT-IDENTIFIER: US 6485950 B1

TITLE: Isozyme of autoclavable superoxide dismutase (SOD), a process for the identification and extraction of the SOD in cosmetic, food and pharmaceutical compositions

DATE-ISSUED: November 26, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kumar; Sanjay	Himachal Pradesh			IN
Sahoo; Rashmita	Himachal Pradesh			IN
Ahuja; Paramvir Singh	Himachal Pradesh			IN

US-CL-CURRENT: 435/189; 424/94.4, 435/183

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	RMC
Draw Desc	Image										

☐ 2. Document ID: US 6465432 B1

L6: Entry 2 of 39

File: USPT

Oct 15, 2002

US-PAT-NO: 6465432

DOCUMENT-IDENTIFIER: US 6465432 B1

**** See image for Certificate of Correction ****

TITLE: Isolated antioxidant peptides form casein and methods for preparing, isolating, and identifying antioxidant peptides

DATE-ISSUED: October 15, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Han; Xiao-Qing	Naperville	IL		
Parkin; Kirk L.	Middleton	WI		
Lincourt; Richard H.	Mundelein	IL		
Gao; Song	Glenview	IL		

US-CL-CURRENT: 514/16; 424/439, 426/34, 435/68.1, 514/12, 514/15, 514/17, 514/18, 530/305, 530/329

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC
Draw Desc	Image										

☐ 3. Document ID: US 6428816 B1

L6: Entry 3 of 39

File: USPT

Aug 6, 2002

US-PAT-NO: 6428816

DOCUMENT-IDENTIFIER: US 6428816 B1

TITLE: Carotenoid agent for inhibiting the conversion of epithelial cells to tumors

DATE-ISSUED: August 6, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schlipalius; Lance Elliot	Ashwood			AU
Buckmeier; Julie A.	Long Beach	CA		
Meyskens, Jr.; Frank L.	Irvine	CA		

US-CL-CURRENT: 424/725; 424/773, 514/725, 514/938

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC
Draw Desc	Image										

☐ 4. Document ID: US 6379697 B1

L6: Entry 4 of 39

File: USPT

Apr 30, 2002

US-PAT-NO: 6379697

DOCUMENT-IDENTIFIER: US 6379697 B1

TITLE: Stabilization of photosensitive materials

DATE-ISSUED: April 30, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gregoriadis; Gregory	London			GB
Loukas; Yannis	Athens			GR

US-CL-CURRENT: 424/450; 514/58

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
Draw Desc	Image									

☐ 5. Document ID: US 6365386 B1

L6: Entry 5 of 39

File: USPT

Apr 2, 2002

US-PAT-NO: 6365386

DOCUMENT-IDENTIFIER: US 6365386 B1

**** See image for Certificate of Correction ****

TITLE: Astaxanthin synthase

DATE-ISSUED: April 2, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hoshino; Tatsuo	Kamakura			JP
Ojima; Kazuyuki	Fujisawa			JP
Setoguchi; Yutaka	Fujisawa			JP

US-CL-CURRENT: 435/183; 435/252.3, 435/320.1, 435/6, 536/23.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KOMIC
Draw Desc	Image									

☐ 6. Document ID: US 6355684 B1

L6: Entry 6 of 39

File: USPT

Mar 12, 2002

US-PAT-NO: 6355684

DOCUMENT-IDENTIFIER: US 6355684 B1

TITLE: Antimicrobial treatment for herpes simplex virus and other infectious diseases

DATE-ISSUED: March 12, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Squires; Meryl	Elmhurst	IL		

US-CL-CURRENT: 514/643; 514/642

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KOMIC
Draw Desc	Image									

☐ 7. Document ID: US 6350784 B1

L6: Entry 7 of 39

File: USPT

Feb 26, 2002

US-PAT-NO: 6350784

DOCUMENT-IDENTIFIER: US 6350784 B1

TITLE: Antimicrobial prevention and treatment of human immunodeficiency virus and other infectious diseases

DATE-ISSUED: February 26, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Squires; Meryl	Willowbrook	IL		

US-CL-CURRENT: 514/642; 514/643

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 8. Document ID: US 6218599 B1

L6: Entry 8 of 39

File: USPT

Apr 17, 2001

US-PAT-NO: 6218599

DOCUMENT-IDENTIFIER: US 6218599 B1

TITLE: Polynucleotide molecule from Haematococcus pluvialis encoding a polypeptide having a .beta.-C-4-oxygenase activity for biotechnological production of (3S, 3'S) astaxanthin and its specific expression in chromoplasts of higher plants

DATE-ISSUED: April 17, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hirschberg; Joseph	Jerusalem			IL
Lotan; Tamar	Kineret			IL

US-CL-CURRENT: 800/295; 435/189, 435/252.3, 435/252.33, 435/254.11, 435/320.1, 435/410, 536/23.1, 536/23.2, 536/23.74, 800/298

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 9. Document ID: US 6180614 B1

L6: Entry 9 of 39

File: USPT

Jan 30, 2001

US-PAT-NO: 6180614

DOCUMENT-IDENTIFIER: US 6180614 B1

TITLE: DNA based vaccination of fish

DATE-ISSUED: January 30, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Davis; Heather L.	Ottawa			CA

US-CL-CURRENT: 514/44; 424/199.1, 424/201.1, 424/202.1, 424/204.1, 424/817, 435/320.1, 435/69.3, 435/69.4, 536/23.1, 536/23.4

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 10. Document ID: US 6138683 A

L6: Entry 10 of 39

File: USPT

Oct 31, 2000

US-PAT-NO: 6138683

DOCUMENT-IDENTIFIER: US 6138683 A

TITLE: Smokeless tobacco products containing antioxidants

DATE-ISSUED: October 31, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hersh; Ted	Atlanta	GA		
Hersh; Rebecca	Atlanta	GA		

US-CL-CURRENT: 131/347; 131/352, 424/439, 424/702, 514/959

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMC
Draw Desc	Image									

☐ 11. Document ID: US 6060324 A

L6: Entry 11 of 39

File: USPT

May 9, 2000

US-PAT-NO: 6060324

DOCUMENT-IDENTIFIER: US 6060324 A

TITLE: Fluorometric assay composition for measurement of antioxidant activity

DATE-ISSUED: May 9, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Naguib; Yousry M. A.	Burlington	MA		

US-CL-CURRENT: 436/71; 436/172

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMC
Draw Desc	Image									

☐ 12. Document ID: US 5965795 A

L6: Entry 12 of 39

File: USPT

Oct 12, 1999

US-PAT-NO: 5965795

DOCUMENT-IDENTIFIER: US 5965795 A

TITLE: Polynucleotide molecule from Haematococcus pluvialis encoding a polypeptide having a beta-C-4-oxygenase activity for biotechnological production of (3S, 3'S) astaxanthin and its specific expression in chromoplasts of higher plants

DATE-ISSUED: October 12, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hirschberg; Joseph	Jerusalem			IL
Lotan; Tamar	Kineret			IL

US-CL-CURRENT: 800/295; 435/183, 435/189, 435/252.3, 435/252.33, 435/254.11,
435/254.21, 435/320.1, 435/410, 536/23.1, 536/23.2, 536/23.74

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 13. Document ID: US 5962018 A

L6: Entry 13 of 39

File: USPT

Oct 5, 1999

US-PAT-NO: 5962018

DOCUMENT-IDENTIFIER: US 5962018 A

**** See image for Certificate of Correction ****

TITLE: Method of treating the skin with organic acids in anhydrous microsphere delivery systems

DATE-ISSUED: October 5, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Curtis; Ernest S.	Milford	PA		
Kalafsky; Robert	Ogdensburg	NJ		
Kaplan; Elinor R.	Paterson	NJ		

US-CL-CURRENT: 424/450; 514/557, 514/574

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 14. Document ID: US 5922346 A

L6: Entry 14 of 39

File: USPT

Jul 13, 1999

US-PAT-NO: 5922346

DOCUMENT-IDENTIFIER: US 5922346 A

TITLE: Antioxidant preparation

DATE-ISSUED: July 13, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hersh; Theodore	Atlanta	GA		

US-CL-CURRENT: 424/439; 424/440, 424/441, 424/464, 424/702, 514/2, 514/904

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 15. Document ID: US 5916791 A

L6: Entry 15 of 39

File: USPT

Jun 29, 1999

US-PAT-NO: 5916791

DOCUMENT-IDENTIFIER: US 5916791 A

TITLE: Polynucleotide molecule from Haematococcus pluvialis encoding a polypeptide having a .beta.--C--4--oxygenase activity for biotechnological production of (3S,3S)astaxanthin

DATE-ISSUED: June 29, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hirschberg; Joseph	93714 Jerusalem			IL
Lotan; Tamar	Moshava			IL

US-CL-CURRENT: 435/189; 435/183, 435/252.3, 435/252.33, 435/325, 435/410, 435/423, 536/23.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMOC
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☐ 16. Document ID: US 5906811 A

L6: Entry 16 of 39

File: USPT

May 25, 1999

US-PAT-NO: 5906811

DOCUMENT-IDENTIFIER: US 5906811 A

TITLE: Intra-oral antioxidant preparations

DATE-ISSUED: May 25, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hersh; Theodore	Atlanta	GA		

US-CL-CURRENT: 424/54; 424/49, 604/58

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMOC
Draw Desc	Image									

☐ 17. Document ID: US 5897871 A

L6: Entry 17 of 39

File: USPT

Apr 27, 1999

US-PAT-NO: 5897871

DOCUMENT-IDENTIFIER: US 5897871 A

TITLE: Therapeutic agent for the treatment of melanomas

DATE-ISSUED: April 27, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schlipalius; Lance Elliott	Ashwood			AU

US-CL-CURRENT: 424/423

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 18. Document ID: US 5876737 A

L6: Entry 18 of 39

File: USPT

Mar 2, 1999

US-PAT-NO: 5876737

DOCUMENT-IDENTIFIER: US 5876737 A

TITLE: Use of salicin as an anti-irritative active compound in cosmetic and topical dermatological preparations

DATE-ISSUED: March 2, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schonrock; Uwe	Nahe			DE
Steckel; Friedhelm	Hamburg			DE
Kux; Ulrich	Urayasu City			JP
Inoue; Kazuo	Naka-Ku			JP

US-CL-CURRENT: 424/401; 424/78.03

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
Draw Desc	Image									

☐ 19. Document ID: US 5834445 A

L6: Entry 19 of 39

File: USPT

Nov 10, 1998

US-PAT-NO: 5834445

DOCUMENT-IDENTIFIER: US 5834445 A

TITLE: Process for preparing decolorized carotenoid-cyclodextrin complexes

DATE-ISSUED: November 10, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sikorski; Christopher	Whiting	IN	46394	
Schwartz; Joel L.	Bethesda	MD	20814	
Shklar; Gerald	Cambridge	MA	02138	

US-CL-CURRENT: 514/58; 514/725, 514/763

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KMIC

☐ 20. Document ID: US 5829449 A

L6: Entry 20 of 39

File: USPT

Nov 3, 1998

US-PAT-NO: 5829449

DOCUMENT-IDENTIFIER: US 5829449 A

TITLE: Smoking products containing antioxidants

DATE-ISSUED: November 3, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hersh; Theodore	Atlanta	GA		
Hersh; Rebecca	Atlanta	GA		

US-CL-CURRENT: 131/202; 131/298, 131/331, 131/334

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KMIC

☐ 21. Document ID: US 5827886 A

L6: Entry 21 of 39

File: USPT

Oct 27, 1998

US-PAT-NO: 5827886

DOCUMENT-IDENTIFIER: US 5827886 A

TITLE: Composition for relief of arthritis-induced symptoms

DATE-ISSUED: October 27, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Herish; Theodore	Atlanta	GA		

US-CL-CURRENT: 514/562; 424/702, 514/162, 514/165, 514/171, 514/474, 514/561, 514/627

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KMIC

☐ 22. Document ID: US 5780448 A

L6: Entry 22 of 39

File: USPT

Jul 14, 1998

US-PAT-NO: 5780448

DOCUMENT-IDENTIFIER: US 5780448 A

TITLE: DNA-based vaccination of fish

DATE-ISSUED: July 14, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Davis; Heather L.	Ottawa			CA

US-CL-CURRENT: 514/44; 424/199.1, 424/201.1, 424/202.1, 424/204.1, 424/227.1,
424/817, 424/93.1, 435/320.1, 435/69.3, 435/69.4, 435/69.5, 536/23.1, 536/23.4,
536/23.72

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMCL
Draw Desc	Image									

☐ 23. Document ID: US 5776441 A

L6: Entry 23 of 39

File: USPT

Jul 7, 1998

US-PAT-NO: 5776441

DOCUMENT-IDENTIFIER: US 5776441 A

TITLE: Lip treatment containing live yeast cell derivative

DATE-ISSUED: July 7, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Scancarella; Neil	Wyckoff	NJ		
Pahlck; Harold	Waldwick	NJ		
Raouf; Maha	Franklin Lakes	NJ		

US-CL-CURRENT: 424/61; 424/401

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMCL
Draw Desc	Image									

☐ 24. Document ID: US 5773026 A

L6: Entry 24 of 39

File: USPT

Jun 30, 1998

US-PAT-NO: 5773026

DOCUMENT-IDENTIFIER: US 5773026 A

TITLE: Aqueous formulations of water-insoluble therapeutic agent comprising carotenoids and/or tocopherols

DATE-ISSUED: June 30, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schlipalius; Lance Elliott	Ashwood			AU

US-CL-CURRENT: 424/450; 424/531, 424/78.02, 514/937

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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☐ 25. Document ID: US 5738868 A

L6: Entry 25 of 39

File: USPT

Apr 14, 1998

US-PAT-NO: 5738868

DOCUMENT-IDENTIFIER: US 5738868 A

TITLE: Liposome compositions and kits therefor

DATE-ISSUED: April 14, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Shinkarenko; Leonid Lurya	Rehovot			IL

US-CL-CURRENT: 424/450; 264/4.1, 264/4.3, 264/4.6, 424/1.21, 424/9.321

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KIMC

☐ 26. Document ID: US 5705180 A

L6: Entry 26 of 39

File: USPT

Jan 6, 1998

US-PAT-NO: 5705180

DOCUMENT-IDENTIFIER: US 5705180 A

TITLE: Therapeutic agent for the treatment of melanomas

DATE-ISSUED: January 6, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schlupalius; Lance Elliott	Ashwood			AU

US-CL-CURRENT: 424/423

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KIMC

☐ 27. Document ID: US 5686488 A

L6: Entry 27 of 39

File: USPT

Nov 11, 1997

US-PAT-NO: 5686488

DOCUMENT-IDENTIFIER: US 5686488 A

TITLE: Polyethoxylated castor oil products as anti-inflammatory agents

DATE-ISSUED: November 11, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gamache; Daniel A.	Arlington	TX		
Graff; Gustav	Cleburne	TX		
Nixon; Jon C.	Mansfield	TX		

US-CL-CURRENT: 514/549; 514/552, 514/914

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

RMIC

☐ 28. Document ID: US 5665553 A

L6: Entry 28 of 39

File: USPT

Sep 9, 1997

US-PAT-NO: 5665553

DOCUMENT-IDENTIFIER: US 5665553 A

TITLE: Methods for determining and modulating cellular redox potential and genotoxic states

DATE-ISSUED: September 9, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Malins; Donald C.	Seattle	WA		

US-CL-CURRENT: 435/6; 435/69.1, 436/501, 436/63, 514/2, 514/44

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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RMIC

☐ 29. Document ID: US 5554374 A

L6: Entry 29 of 39

File: USPT

Sep 10, 1996

US-PAT-NO: 5554374

DOCUMENT-IDENTIFIER: US 5554374 A

TITLE: Skin preparation using nanospheres

DATE-ISSUED: September 10, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Olivier-Terras; Josette	Peronnas			FR

US-CL-CURRENT: 424/401; 424/450, 424/491, 424/59, 424/60, 514/844

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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☐ 30. Document ID: US 5023271 A

L6: Entry 30 of 39

File: USPT

Jun 11, 1991

US-PAT-NO: 5023271

DOCUMENT-IDENTIFIER: US 5023271 A

TITLE: Pharmaceutical microemulsions

DATE-ISSUED: June 11, 1991

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Vigne; Jean-Louis	San Francisco	CA		
Kane; John P.	Hillsborough	CA		

US-CL-CURRENT: 514/458; 514/168, 514/546, 514/547, 514/589, 514/681, 514/725, 514/788

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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L6: Entry 31 of 39

File: USPT

Apr 16, 1991

US-PAT-NO: 5008102

DOCUMENT-IDENTIFIER: US 5008102 A

TITLE: Biocompatible intraocular light-screening compositions and methods of intraocular light screening

DATE-ISSUED: April 16, 1991

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
York; Kenneth K.	Los Angeles	CA	90027	

US-CL-CURRENT: 424/59; 351/160H, 351/160R, 351/161, 351/162, 351/163, 427/2.24, 514/912, 514/914, 623/6.57, 623/6.61

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMIC
Draw Desc	Image										

☐ 32. Document ID: WO 9413265 A1

L6: Entry 32 of 39

File: EPAB

Jun 23, 1994

PUB-NO: WO009413265A1

DOCUMENT-IDENTIFIER: WO 9413265 A1

TITLE: A FREE RADICAL QUENCHING LIPOSOMAL COMPOSITION

PUBN-DATE: June 23, 1994

INVENTOR-INFORMATION:

NAME	COUNTRY
SMITH, MILTON G	US

INT-CL (IPC): A61K 9/127

EUR-CL (EPC): A61K007/00; A61K009/127, A61K031/355 , A61K031/375 , A61K033/24 , A61K033/30 , A61K033/32 , A61K033/34 , A61K007/40 , A61K038/06

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMIC
Draw Desc	Clip Img	Image									

☐ 33. Document ID: RU 2164794 C1

L6: Entry 33 of 39

File: DWPI

Apr 10, 2001

DERWENT-ACC-NO: 2001-334321

DERWENT-WEEK: 200135

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TITLE: Substance lipovitam-beta, liposomal carotene, vitamin complex and method of its preparing

INVENTOR: KORENEVA, O A; SAPOZHKOVA, S M ; VAINSHTEIN, V A ; VLASENKO I YU,

PRIORITY-DATA: 1999RU-0115055 (July 19, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
RU 2164794 C1	April 10, 2001		000	A61K009/20

INT-CL (IPC): A61 K 9/20; A61 K 9/22; A61 K 31/07; A61 K 31/355; A61 K 31/375; A61 P 3/02

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC
Draw Desc	Image										

☐ 34. Document ID: DE 29607273 U1

L6: Entry 34 of 39

File: DWPI

Jun 20, 1996

DERWENT-ACC-NO: 1996-288393

DERWENT-WEEK: 199630

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TITLE: Plant extract complex for skin care - comprises e.g. vitamin=E, tea-tree oil, aloe vera and geranium oil

PRIORITY-DATA: 1996DE-2007273 (April 23, 1996)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
DE 29607273 U1	June 20, 1996		005	A61K007/48

INT-CL (IPC): A61 K 7/48

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
Draw Desc	Image									

☐ 35. Document ID: WO 9413265 A1 AU 9457482 A EP 673241 A1 EP 673241 A4

L6: Entry 35 of 39

File: DWPI

Jun 23, 1994

DERWENT-ACC-NO: 1994-217495

DERWENT-WEEK: 199842

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TITLE: New free radical quenching compsn. with cosmetic and clinical uses - contains antioxidants e.g. beta-carotene, vitamin=E, vitamin=C, glutathione and niacin, opt. with trace metal

INVENTOR: SMITH, M G

PRIORITY-DATA: 1992US-0989593 (December 11, 1992)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 9413265 A1	June 23, 1994	E	029	A61K009/127
AU 9457482 A	July 4, 1994		000	A61K009/127
EP 673241 A1	September 27, 1995	E	000	A61K009/127
EP 673241 A4	October 15, 1997		000	A61K009/127

INT-CL (IPC): A61K 9/127

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KM/C
Draw Desc	Image									

☐ 36. Document ID: WO 9313742 A1 AU 672191 B FR 2686249 A1 AU 9334553 A EP 625039 A1 JP 07505862 W EP 625039 B1 DE 69300521 E ES 2080621 T3 US 5554374 A

L6: Entry 36 of 39

File: DWPI

Jul 22, 1993

DERWENT-ACC-NO: 1993-242870

DERWENT-WEEK: 199646

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TITLE: New compsns. for melanic skin stains - contg. excipients, encapsulated beta carotene, and mixt. of UV-A and UV-B sun filters

INVENTOR: OLIVIER-TERRAS, J; OLIVIER, J

PRIORITY-DATA: 1992FR-0000619 (January 16, 1992)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 9313742 A1	July 22, 1993	F	022	A61K007/00
AU 672191 B	September 26, 1996		000	A61K007/42
FR 2686249 A1	July 23, 1993		012	A61K007/40
AU 9334553 A	August 3, 1993		000	A61K007/00
EP 625039 A1	November 23, 1994	F	000	A61K007/00
JP 07505862 W	June 29, 1995		000	A61K007/42
EP 625039 B1	September 20, 1995	F	007	A61K007/00
DE 69300521 E	October 26, 1995		000	A61K007/00
ES 2080621 T3	February 1, 1996		000	A61K007/00
US 5554374 A	September 10, 1996		004	A61K007/48

INT-CL (IPC): A61 K 7/00; A61 K 7/40; A61 K 7/42; A61 K 7/48; A61 K 9/51; A61 K 31/015

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KM/C
Draw Desc	Image									

☐ 37. Document ID: EP 386680 A AU 9051950 A WO 9010430 A ZA 9001675 A

L6: Entry 37 of 39

File: DWPI

Sep 12, 1990

DERWENT-ACC-NO: 1990-276733

DERWENT-WEEK: 199037

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TITLE: Compsn. contg. liposome-melanin complex - useful for sunless tanning of skin

INVENTOR: AGIN, P P

PRIORITY-DATA: 1989US-0320012 (March 7, 1989)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 386680 A	September 12, 1990		000	
AU 9051950 A	October 9, 1990		000	
WO 9010430 A	September 20, 1990		000	
ZA 9001675 A	November 28, 1990		000	

INT-CL (IPC): A61K 7/00

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMOC
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☐ 38. Document ID: FR 2596986 A

L6: Entry 38 of 39

File: DWPI

Oct 16, 1987

DERWENT-ACC-NO: 1987-343748

DERWENT-WEEK: 198749

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TITLE: Topical compsns. contg. lactoferrin - combat free radicals and are effective against skin ageing, inflammations and erythema

INVENTOR: GREFF, D

PRIORITY-DATA: 1986FR-0005183 (April 11, 1986)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
FR 2596986 A	October 16, 1987		004	

INT-CL (IPC): A61K 7/48; C07K 15/06

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMOC
Draw Desc	Image									

☐ 39. Document ID: EP 229561 A JP 2855105 B2 FR 2591105 A JP 62215513 A ES 2003605 A US 5034228 A CA 1298195 C EP 229561 B1 DE 3686325 G JP 93015689 B JP 09110669 A

L6: Entry 39 of 39

File: DWPI

Jul 22, 1987

DERWENT-ACC-NO: 1987-200045

DERWENT-WEEK: 199911

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TITLE: Pharmaceutical or cosmetic compsns. contg. retinoid cpds. - encapsulated in liposome(s) which reduces skin irritant effects

INVENTOR: MEYBECK, A; MICHELON, P ; MONTASTIER, C ; REDZINIAK, G

PRIORITY-DATA: 1985FR-0018362 (December 11, 1985)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 229561 A	July 22, 1987	F	019	
JP 2855105 B2	February 10, 1999		003	A61K007/00
FR 2591105 A	June 12, 1987		000	
JP 62215513 A	September 22, 1987		000	
ES 2003605 A	November 1, 1988		000	
US 5034228 A	July 23, 1991		008	
CA 1298195 C	March 31, 1992		000	
EP 229561 B1	August 5, 1992	F	021	A61K009/50
DE 3686325 G	September 10, 1992		000	A61K009/50
JP 93015689 B	March 2, 1993		010	A61K007/48
JP 09110669 A	April 28, 1997		009	A61K007/48

INT-CL (IPC): A61K 7/00; A61K 7/06; A61K 7/42; A61K 7/48; A61K 9/127; A61K 9/50; A61K 31/015; A61K 31/07; A61K 37/22

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMC
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Terms	Documents
\$scarotene same liposome\$	39

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WEST Search History

DATE: Tuesday, July 29, 2003

Set Name **Query**
side by side

Hit Count **Set Name**
result set

DB=USPT,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR

L6	\$carotene same liposome\$	39	L6
L5	lycopene same liposome\$	2	L5
L4	(saturated adj2 solution) same liposome\$	16	L4
L3	(saturated adj5 phospholipid adj5 solution) same liposome\$	1	L3
L2	(saturated adj2 phospholipid adj2 solution) same liposome\$	1	L2
L1	carotenoid\$ same liposome\$	29	L1

END OF SEARCH HISTORY

WEST Search History

DATE: Tuesday, July 29, 2003

<u>Set Name</u> side by side	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u> result set
<i>DB=USPT,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR</i>			
L5	liposomes same (astaxanthin or lutein)	2	L5
L4	L3 and (method adj3 prepar\$)	111	L4
L3	L2 and (hydrophobic or lipophilic)	172	L3
L2	L1 and liposome\$	258	L2
L1	phospholipid\$ adj3 solution	517	L1

END OF SEARCH HISTORY

WEST

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L4: Entry 60 of 111

File: USPT

Jan 13, 1998

DOCUMENT-IDENTIFIER: US 5707608 A

TITLE: Methods of making liposomes containing hydro-monobenzoporphyrin photosensitizerAbstract Text (1):

Liposomal compositions containing green porphyrins as photosensitizers are improved by enhancing the ratio of phospholipid to photosensitizer and by conducting the hydration and sizing of the liposomes in the composition at low temperature.

Brief Summary Text (2):

The invention relates to improved pharmaceutical compositions comprising liposomes incorporating porphyrin photosensitizers and methods for making these liposomes. Specifically, the invention is directed to pharmaceutical liposome compositions comprising a hydro-monobenzo-porphyrin photosensitizer and a mixture of phospholipids comprising egg phosphatidyl glycerol ("EPG") and dimyristoyl phosphatidyl choline ("DMPC") in a photosensitizer:phospholipid molar ratio of about 1:7.0 or more phospholipid. The liposomes are made in such a way that the particle size range is about 150 to 300 nm.

Brief Summary Text (3):

The photosensitizing liposome compositions are useful to mediate the destruction of unwanted cells or tissues or other undesirable materials by irradiation or to detect their presence through fluorescence. Particularly preferred hydro-monobenzoporphyrin photosensitizers used in the practice of this invention include those having one or more light absorption maxima in the range of 670-780 nm.

Brief Summary Text (9):

While the porphyrin compounds have a natural ability to localize in neoplastic tissue, while being cleared from the normal surrounding tissue, the selectivity of the porphyrin photosensitizers is still somewhat limited. Because tumor tissue generally includes a number of different components, such as malignant cells, a vascular system, macrophages, fibroblasts, etc., the distribution of the photosensitizer within tumor tissue may be highly heterogeneous. This is especially true for those photosensitizers that are not homogeneous and that contain a mixture of components having different degrees of hydro- or liposolubility. Zhou et al., Photochemistry and Photobiology, 48:487-92 (1988). The low selectivity of some of these agents as tumor localizers may lead to side-effects, such as an undesirably systemic hypersensitivity to light. Therefore, an active area of research has been to increase the tumor selectivity of known porphyrin photosensitizers and to identify those porphyrin photosensitizers that may exhibit greater tumor-selectivity. In general, photosensitizers that are more lipophilic tend to exhibit greater tumor-targeting capability. Spikes et al., Lasers in Medical Science, 2:3, 3-15 (1986).

Brief Summary Text (10):

It has recently been shown that the encapsulation of certain drugs in liposomes, prior to administration, has a marked effect on the pharmacokinetics, tissue distribution, metabolism and efficacy of the therapeutic agent. In an effort to increase the tumor selectivity of porphyrin photosensitizers, porphyrin compounds have been incorporated into unilamellar liposomes, resulting in a larger accumulation and a more prolonged retention of the photosensitizer by both cultured malignant cells and in experimental tumors in vivo. Jori et al., Br. J. Cancer, 48:307-309

(1983); Cozzani et al., In Porphyrins in Tumor Phototherapy, 177-183, Plenum Press (Andreoni et al. eds. 1984). This more efficient targeting of tumor tissues by liposome-associated porphyrins may be due in part to the specific delivery of phospholipid vesicles to serum lipoproteins, which have been shown to interact preferentially with hyperproliferative tissue, such as tumors, through receptor-mediated endocytosis. In this manner, the selectivity of porphyrin uptake by tumors has been increased, as compared with photosensitizers dissolved in aqueous solution. See Zhou et al., supra.

Brief Summary Text (11):

Accordingly, hematoporphyrin and hematoporphyrin dimethyl esters have been formulated in unilamellar vesicles of dipalmitoyl phosphatidyl choline (DPPC) and liposomes of dimyristoyl (DMPC) and distearoyl phosphatidyl choline (DSPC). Zhou et al., supra; Ricchelli, New Directions in Photodynamic Therapy, 847:101-106 (1987); Milanesi, Int. J. Radiat. Biol., 55:59-69 (1989). Similarly, HP, Photofrin.RTM., porfimer sodium, and tetrabenzoporphyrins have been formulated in liposomes composed of egg phosphatidyl choline (EPC). Johnson et al., Proc. Photodynamic Therapy: Mechanisms II, Proc. SPIE-Int. Soc. Opt. Eng., 1203:266-80 (1990). Further, freeze-dried pharmaceutical formulations comprising a porphyrin photosensitizer, a disaccharide or polysaccharide, and one or more phospholipids (such as EPG and DMPC) have been made. These formulations form liposomes containing an effective amount of porphyrin photosensitizer upon reconstitution with a suitable aqueous vehicle and are described in Desai et al., copending U.S. application Ser. No. 08/489,850 filed 13 Jun. 1995.

Brief Summary Text (13):

Farmer et al., U.S. Pat. No. 4,776,991 discloses the large-scale encapsulation of hemoglobin in liposomes having a narrow liposome size distribution comprising, as phospholipids,

Brief Summary Text (18):

(Farmer et al., column 3, lines 52-69.) These lipids are mixed in chloroform to form a solution; the chloroform is evaporated away to form a lipid film; and sterile hemoglobin is added to the film with gentle agitation at 35.degree. C. (30.degree.-37.degree. C.) for 45 minutes to form multilamellar liposomes. Rotary agitation of the liposomes is continued at 4.degree. C. (2.degree.-6.degree. C.) for 10-16 hours, and the liposomes are forced through a Microfluidizer.TM. to break multilamellar liposomes and produce large unilamellar liposomes. The interaction cheer of the Microfluidizer.TM. is maintained at 5.degree.-7.degree. C. (Column 4, lines 1-14; column 7, lines 3-9 and 19-21.) The lipids chosen to make the liposomes, however, must be temporarily shrunk by hyperosmotic shock with added saline prior to sterilization by pressure filtration through a standard 0.22 .mu.m sterilizing filter. (Column 4, line 18-22; column 9, lines 55-58.)

Brief Summary Text (19):

Kappas et al., U.S. Pat. No. 5,010,073 issued 23 Apr. 1991, discloses the preparation of liposomes containing a metalloporphyrin with egg phosphatidyl choline ("EPC") being used as the lipid. The EPC is dissolved in chloroform, the metalloporphyrin is added, and the solution is evaporated to dryness. Phosphate buffered saline at room temperature is used to hydrate the lipid film, and the mixture is "vortexed vigorously." Solids are collected by centrifuging at 4.degree. C. The weight ratio of EPC to metalloporphyrin may be greater than 10. (Kappas et al., column 6, lines 46-65.) However, Kappas et al. recommends that the resulting metalloporphyrin liposomes be sonicated prior to injection to prevent the production of large aggregates. (Column 6, line 66 through column 7, line 1.)

Brief Summary Text (20):

Schneider et al., U.S. Pat. No. 5,270,053 issued 14 Dec. 1993, discloses liposome formulations said to be free of solid particles and larger lipid aggregates. (Schneider et al., column 3, lines 52-54.) However, the presence of a specific synthetic lipid is required. (Column 2, lines 51-66.) For example, in Example 21, at columns 13 and 14, 50 grams of a mixture of two such synthetic lipids are dissolved in tertiary butanol, which is then mixed with a solution of 0.5 g zinc-phthalocyanine. Using a dynamic mixer, the solution is mixed with 10 liters of lactose medium cooled to 4.degree. C. to produce a blue, slightly opalescent dispersion. The separation and isolation of large liposomes from the small liposomes

is performed, when necessary, by conventional separation methods such as gel filtration or sedimentation. (Column 7, lines 11-17.)

Brief Summary Text (21):

Thus, there remains a need for a large-scale method to produce DMPC/EPG liposomes containing a photosensitizer in small enough particle sizes that large quantities of pharmaceutical compositions containing the liposomes are easily aseptically filtered through standard 0.22 μm sterilizing filters in an efficient manner and without the need for preparing the synthetic lipids of Kappas et al.

Brief Summary Text (23):

The present invention involves a method for making a pharmaceutical composition containing liposomes. The liposomes comprise a therapeutically acceptable amount of a hydro-monobenzoporphyrin photosensitizer and a mixture of phospholipids comprising egg phosphatidyl glycerol ("EPG") and dimyristoyl phosphatidyl choline ("DMPC"). The method of making such liposomes comprises the steps of:

Brief Summary Text (26):

c. hydrating the lipid film with an aqueous solution at a temperature below 30.degree. C., to form coarse liposomes containing a photosensitizer-phospholipid complex; and

Brief Summary Text (27):

d. homogenizing or reducing the particle size of the coarse liposomes to a particle size range of about 150 to 300 nm at a temperature below about 30.degree. C.

Brief Summary Text (29):

Maintaining the hydration temperature and the homogenizing/reducing step at a temperature below 30.degree. C. would not have been expected to produce smaller particle sizes. In fact, the invention is contrary to the conventional wisdom that small particle sizes are achieved by increasing rather than decreasing these temperatures. See, e.g., M. Lee et al., "Size Distribution of Liposomes by Flow Field-Flow Fractionation", J. Pharm. & Biomed. Analysis, 11:10, 911-20 (1993), equation (6) showing particle diameter "d" as inversely related to temperature "T", and FIG. 6b showing liposome preparation I (prepared at about 70.degree. C.) having smaller particle sizes than preparation II (prepared at about 23.degree. C.).

Brief Summary Text (30):

The invention also contemplates the pharmaceutical compositions themselves, which comprise liposomes including a hydro-monobenzoporphyrin photosensitizer and a mixture of DMPC and EPG phospholipids in a photosensitizer-phospholipid molar ratio of about 1:7.0 or more phospholipid, and which have a particle size of about 150 to 300 nm.

Brief Summary Text (31):

These liposome compositions provide nearly 100% encapsulation of the hydro-monobenzoporphyrin photosensitizer, which can be expensive and usually requires a complicated synthetic procedure to produce. Thus, there is no reworking necessary and very little waste of the photosensitizer. In addition, due to their small particle size, the present liposomes exhibit the improved filterability important in producing large-scale batches of a 500 ml to liter or more, as well as improved retention of photosensitizer potency.

Detailed Description Text (2):

The present invention relates to a pharmaceutical liposome formulation of a hydro-monobenzoporphyrin photosensitizer for use in the photodynamic therapy or diagnosis of tumors, or for a variety of other therapeutic applications. Liposomes are completely closed, lipid bilayer membranes that contain an entrapped aqueous volume. Typically, liposomes are formed spontaneously upon the addition of an aqueous solution to a dry lipid film.

Detailed Description Text (3):

The liposomes of the invention may be unilamellar vesicles having a single membrane bilayer or multilamellar vesicles having multiple membrane bilayers, each bilayer being separated from the next by an aqueous layer. A liposome bilayer is composed of two lipid monolayers having a hydrophobic "tail" region and a hydrophilic "head"

region. The structure of the membrane bilayer is such that the hydrophobic (nonpolar) "tails" of the lipid monolayers orient themselves towards the center of the bilayer, while the hydrophilic "heads" orient themselves toward the aqueous phase. Either unilamellar or multilamellar or other types of liposomes may be used in the practice of the present invention.

Detailed Description Text (4):

In a liposome-drug delivery system, a hydrophilic therapeutic agent can be entrapped in the aqueous phase of the liposome and then administered to the patient. Alternatively, if the therapeutic agent is lipophilic, it may associate with the lipid bilayer. Liposomes may be used to help "target" a drug to an active site or to solubilize hydrophobic drugs for parenteral administration. Typically, the hydro-monobenzoporphyrin photosensitizer of the invention is relatively hydrophobic and forms a stable photosensitizer-lipid complex.

Detailed Description Text (5):

The liposomes of the present invention possess certain attributes that make them well-suited for delivering a hydro-monobenzoporphyrin photosensitizer. The liposomes formed in the present invention are "fast breaking" in that the photosensitizer-liposome combination is stable in vitro but, when administered in vivo, the photosensitizer is rapidly released into the bloodstream where it associates with serum lipoproteins. It is believed that this inhibits the photosensitizer from being accumulated in non-target tissues such as the liver.

Detailed Description Text (16):

Many desirable hydro-monobenzoporphyrin photosensitizers, such as BPD-MA, are not only insoluble in water at physiological pH's, but are also insoluble in (1) pharmaceutically acceptable aqueous-organic co-solvents, (2) aqueous polymeric solutions, and (3) surfactant/micellar solutions. However, such photosensitizers can still be "solubilized" in a form suitable for parenteral administration by using a liposome composition. For example, BPD-MA can be "solubilized" at a concentration of about 2.0 mg/ml in aqueous solution using an appropriate mixture of phospholipids to form encapsulating liposomes.

Detailed Description Text (18):

The liposomes of the inventions comprise a mixture of the commonly encountered lipids dimyristoyl phosphatidyl choline ("DMPC") and egg phosphatidyl glycerol ("EPG"). The presence of DMPC is important because DMPC is the major component in the composition to form liposomes which can solubilize and encapsulate insoluble hydro-monobenzoporphyrin photosensitizers into a lipid bilayer. The presence of EPG is important because the negatively charged, polar head group of this lipid can prevent aggregation of the liposomes.

Detailed Description Text (19):

Other phospholipids, in addition to DMPC and EPG, may also be present. Examples of suitable additional phospholipids that may also be incorporated into the liposomes of the present invention include phosphatidyl cholines (PCs), including mixtures of dipalmitoyl phosphatidyl choline (DPPC) and distearoyl phosphatidyl choline (DSPC). Examples of suitable phosphatidyl glycerols (PGs) include dimyristoyl phosphatidyl glycerol (DMPG), DLPG and the like.

Detailed Description Text (21):

The molar ratio of the hydro-monobenzoporphyrin photosensitizer to the DMPC/EPG phospholipid mixture can be as low as 1:7.0 or may contain a higher proportion of phospholipid, such as 1:7.5. Preferably, this molar ratio is 1:8 or more phospholipid, such as 1:10, 1:15, or 1:20. This molar ratio depends upon the exact photosensitizer being used, but will assure the presence of a sufficient number of DMPC and EPG lipid molecules to form a stable complex with most hydro-monobenzoporphyrin photosensitizer molecules. When the number of lipid molecules is not sufficient to form a stable complex, the lipophilic phase of the lipid bilayer becomes saturated with photosensitizer molecules. Then, any slight change in the process conditions can force some of the previously encapsulated photosensitizer to leak out of the vesicle, onto the surface of the lipid bilayer, or even out into the aqueous phase.

Detailed Description Text (22):

If the concentration of hydro-monobenzoporphyrin photosensitizer is high enough, it can actually precipitate out from the aqueous layer and promote aggregation of the liposomes. The more unencapsulated photosensitizer that is present, the higher the degree of aggregation. The more aggregation, the larger the mean particle size will be, and the more difficult aseptic or sterile filtration will be. Thus, as demonstrated in Example 1 below, even small changes in the molar ratio can be important in achieving the improved filterability sought in the invention.

Detailed Description Text (23):

Accordingly, slight increases in the lipid content can increase significantly the filterability of the liposome composition by increasing the ability to form and maintain small particles. This is particularly advantageous when working with significant volumes of 500 ml, a liter, five liters, 40 liters, or more, as opposed to smaller batches of about 100-500 ml or less. This volume effect is thought to occur because larger homogenizing devices tend to provide less efficient agitation than can be accomplished easily on a small scale. For example, a large size Microfluidizer.TM. has a less efficient interaction chamber than that one of a smaller size.

Detailed Description Text (27):

In an especially preferred embodiment, the particular combination of the phospholipids, DMPC and EPG, and a disaccharide or polysaccharide form a liposomal composition having liposomes of a particularly narrow particle size distribution. When the process of hydrating a lipid film is prolonged, larger liposomes tend to be formed, or the photosensitizer can even begin to precipitate. The addition of a disaccharide or polysaccharide provides instantaneous hydration and the largest surface area for depositing a thin film of the drug-phospholipid complex. This thin film provides for faster hydration so that, when the liposome is initially formed by adding the aqueous phase, the liposomes formed are of a smaller and more uniform particle size. This provides significant advantages in terms of manufacturing ease.

Detailed Description Text (29):

Disaccharides or polysaccharides are preferred to monosaccharides for this purpose. To keep the osmotic pressure of the liposome composition of the invention similar to that of blood, no more than 4-5% monosaccharides could be added. In contrast, about 9-10% of a disaccharide can be used without generating an unacceptable osmotic pressure. The higher amount of disaccharide provides for a larger surface area, which results in smaller particle sizes being formed during hydration of the lipid film.

Detailed Description Text (30):

Accordingly, the preferred liposomal composition of the present invention comprises a disaccharide or polysaccharide, in addition to the photosensitizer and the mixture of DMPC and EPG phospholipids. When present, the disaccharide or polysaccharide is preferably chosen from among the group consisting of lactose, trehalose, maltose, maltotriose, palatinose, lactulose or sucrose, with lactose or trehalose being preferred. Even more preferably, the liposomes comprise lactose or trehalose.

Detailed Description Text (32):

The presence of the disaccharide or polysaccharide in the composition not only tends to yield liposomes having extremely small and narrow particle size ranges, but also provides a liposome composition in which hydro-monobenzoporphyrin photosensitizers, in particular, may be stably incorporated in an efficient manner, i.e., with an encapsulation efficiency approaching 80-100%. Moreover, liposomes made with a saccharide typically exhibit improved physical and chemical stability, such that they can retain an incorporated hydro-monobenzoporphyrin photosensitizer compound without leakage upon prolonged storage, either as a reconstituted liposomal suspension or as a cryodesiccated powder.

Detailed Description Text (36):

Liposomes containing a selected hydro-monobenzoporphyrin photosensitizer as described herein may be prepared by combining the photosensitizer and the DMPC and EPG phospholipids (and any other optional phospholipids or excipients, such as antioxidants) in the presence of an organic solvent. Suitable organic solvents include any volatile organic solvent, such as diethyl ether, acetone, methylene

chloride, chloroform, piperidine, piperidine-water mixtures, methanol, tert-butanol, dimethyl sulfoxide, N-methyl-2-pyrrolidone, and mixtures thereof. Preferably, the organic solvent is water-immiscible, such as methylene chloride, but water immiscibility is not required. In any event, the solvent chosen should not only be able to dissolve all of the components of the lipid film, but should also not react with, or otherwise deleteriously affect, these components to any significant degree.

Detailed Description Text (39):

Upon hydration, coarse liposomes are formed that incorporate a therapeutically effective amount of the hydro-monobenzoporphyrin photosensitizer-phospholipid complex. The "therapeutically effective amount" can vary widely, depending on the tissue to be treated and whether it is coupled to a target-specific ligand, such as an antibody or an immunologically active fragment. It should be noted that the various parameters used for selective photodynamic therapy are interrelated. Therefore, the therapeutically effective amount should also be adjusted with respect to other parameters, for example, fluence, irradiance, duration of the light used in photodynamic therapy, and the time interval between administration of the photosensitizing agent and the therapeutic irradiation. Generally, all of these parameters are adjusted to produce significant damage to tissue deemed undesirable, such as neovascular or tumor tissue, without significant damage to the surrounding tissue, or to enable the observation of such undesirable tissue without significant damage to the surrounding tissue.

Detailed Description Text (42):

In accordance with the usual expectation that the aqueous solubility of a substance should increase as higher temperatures are used, at a temperature around the transition temperature of the complex, the lipid membrane tends to undergo phase transition from a "solid" gel state to a pre-transition state and, finally, to a more "fluid" liquid crystal state. At these higher temperatures, however, not only does fluidity increase, but the degree of phase separation and the proportion of membrane defects also increases. This results in an increasing degree of leakage of the photosensitizer from inside the membrane to the interface and even out into the aqueous phase. Once a significant amount of liposome leakage has occurred, even slight changes in the conditions such as a small drop in temperature, can shift the equilibrium away from aqueous "solubility" in favor of precipitation of the photosensitizer. Moreover, once the typically water-insoluble photosensitizer begins to precipitate, it is not possible to re-encapsulate it within the lipid bilayer. The precipitate is thought to contribute significantly to filterability problems.

Detailed Description Text (43):

In addition, the usual thickness of a lipid bilayer in the "solid" gel state (about 47 .ANG.) decreases in the transition to the "liquid" crystalline state to about 37 .ANG., thus shrinking the entrapped volume available for the hydro-monobenzoporphyrin photosensitizer to occupy. The smaller "room" is not capable of containing as great a volume of photosensitizer, which can then be squeezed out of the saturated lipid bilayer interstices. Any two or more vesicles in the process of exuding photosensitizer may aggregate together, introducing further difficulties with respect to particle size reduction and ease of sterile filtration. See FIG. 4 for an illustration of one proposed mechanism to explain this surprising effect of temperature on photosensitizer liposome aggregation. Moreover, the use of higher hydration temperatures, such as, for example, about 35.degree. to 45.degree. C., can also result in losses of photosensitizer potency as the photosensitizer either precipitates or aggregates during aseptic filtration.

Detailed Description Text (44):

The particle sizes of the coarse liposomes first formed in hydration are then homogenized to a more uniform size, reduced to a smaller size range, or both, to about 150 to 300 nm, preferably also at a temperature that does not exceed about 30.degree. C., preferably below the glass transition temperature of the photosensitizer-phospholipid complex formed in the hydration step, and even more preferably below room temperature of about 25.degree. C. Various high-speed agitation devices may be used during the homogenization step, such as a Microfluidizer.TM., for example a Microfluidics.TM. Model 110F; a sonicator; a high-shear mixer; a homogenizer; or a standard laboratory shaker.

Detailed Description Text (45):

It has been found that the homogenization temperature should be at room temperature or lower, e.g., 15.degree.-20.degree. C. At higher homogenization temperatures, such as about 32.degree.-42.degree. C., the relative filterability of the liposome composition may improve initially due to increased fluidity as expected, but then, unexpectedly, tends to decrease with continuing agitation due to increasing particle size.

Detailed Description Text (47):

However, as the number of passes and the temperature both increase, more of the hydrophobic hydro-monobenzoporphyrin photosensitizer molecules are squeezed out of the liposomes, increasing the tendency of the liposomes to aggregate into larger particles. At the point at which the aggregation of vesicles begins to dominate the process, the sizes cannot be reduced any further. Surprisingly, particle sizes actually then tend to grow through aggregation.

Detailed Description Text (49):

As a last step, the compositions of the inventions are preferably aseptically filtered through a filter having an extremely small pore size, i.e., 0.22 .mu.m. Filter pressures used during sterile filtration can vary widely, depending on the volume of the composition, the density, the temperature, the type of filter, the filter pore size, and the particle size of the liposomes. However, as a guide, a typical set of filtration conditions would be as follows: filtration pressure of 15-25 psi; filtration load of 0.8 to 1.5 ml/cm.sup.2 ; and filtration temperature of about 25.degree. C.

Detailed Description Text (51):

(1) Sterile filtration of organic solvent through a hydrophobic, 0.22 .mu.m filter.

Detailed Description Text (53):

(3) Filtration of the resulting solution through a 0.22 .mu.m hydrophobic filter.

Detailed Description Text (59):

(9) Hydration of the lipid film with a 10% lactose solution to form coarse liposomes.

Detailed Description Text (60):

(10) Reduction of the particle sizes of the coarse liposomes by passing them through a Microfluidizer.TM. three times.

Detailed Description Text (61):

(11) Determination of the reduced particle size distribution of liposomes.

Detailed Description Text (62):

(12) Aseptic filtration of the liposome composition through a 0.22 .mu.m hydrophilic filter. (Optionally, the solution may first be pre-filtered with a 5.0 .mu.m pre-filter.)

Detailed Description Text (64):

(14) Filling of vials with the liposome composition.

Detailed Description Text (67):

Once formulated, the liposome composition of the invention may be freeze-dried for long-term storage if desired. For example, BPD-MA, a preferred hydro-monobenzoporphyrin photosensitizer, has maintained its potency in a cryodesiccated liposome composition for a period of at least nine months at room temperature, and a shelf life of at least two years has been projected. If the composition is freeze-dried, it may be packed in vials for subsequent reconstitution with a suitable aqueous solution, such as sterile water or sterile water containing a saccharide and/or other suitable excipients, prior to administration, for example, by injection.

Detailed Description Text (68):

Preferably, liposomes that are to be freeze-dried are formed upon the addition of an aqueous vehicle contain a disaccharide or polysaccharide during hydration. The

composition is then collected, placed into vials, freeze-dried, and stored, ideally under refrigeration. The freeze-dried composition can then be reconstituted by simply adding water for injection just prior to administration.

Detailed Description Text (70):

The liposomal composition of the present invention provides liposomes of a sufficiently small and narrow particle size that the aseptic filtration of the composition through a 0.22 μm hydrophilic filter can be accomplished efficiently and with large volumes of 500 ml to a liter or more without significant clogging of the filter. A particularly preferred particle size range is below about 300 nm, more preferably below from about 250 nm. Most preferably, the particle size is below about 220 nm.

Detailed Description Text (71):

As seen above, the invention controls three major parameters that can affect the ease of particle size reduction to an unexpected degree. As a result, the filterability, particularly with standard aseptic filtration, is significantly improved in the liposome composition of the invention. These parameters are (1) suitable molar ratio of hydro-monobenzoporphyrin photosensitizer to DMPC-EPG lipid mixture; (2) temperature during the hydration step; and (3) temperature during the homogenization or size reduction step. Of these three factors, the photosensitizer/lipid molar ratio appears to have the greatest effect.

Detailed Description Text (72):

Filterability can be tested by passing a liposome composition through a Microfluidizer.TM. three times and withdrawing a sample with a syringe. The syringe is connected to a 0.22 μm hydrophilic filter and then placed in a syringe pump. The constant rate of piston movement is set at 10 ml/min, and filtrate is collected until the filter becomes blocked by large aggregates of liposome. The volume of the filtrate is then measured and recorded in terms of ml/cm.² or g/cm.², with a square centimeter being the effective filtration area. Thus, filterability for the purposes of the invention is defined as the maximum volume or weight of liposomal composition that can be filtered through a 0.22 μm filter.

Detailed Description Text (74):

The use of the hydro-monobenzoporphyrin photosensitizers incorporated in the liposomes of the invention is typically for the diagnosis or treatment of cancer. The liposomal compositions are useful in sensitizing neoplastic cells or other abnormal tissue, including infectious agents, to destruction by exposure with light, preferably, visible light. Upon photoactivation, the photosensitizer thought to promote the formation of singlet oxygen, which is responsible for the cytotoxic effect. By incorporating the photosensitizer in the liposomes of the present invention, more efficient sensitization of tumor tissues can be obtained.

Detailed Description Text (76):

Generally speaking, the concentration of the hydro-monobenzoporphyrin photosensitizer in the liposome depends upon the nature of the photosensitizer used. When BPD-MA is used, for example, the photosensitizer is generally incorporated in the liposomes at a concentration of about 0.10% up to 0.5% w/v. If freeze-dried and reconstituted, this would typically yield a reconstituted solution of up to about 5.0 mg/ml photosensitizer.

Detailed Description Text (77):

The liposome compositions of the invention are typically administered parenterally. Injection may be intravenous, subcutaneous, intramuscular, intrathecal, or even intraperitoneal. However, the liposomes could also be administered by aerosol intranasally or intrapulmonarily.

Detailed Description Text (78):

The quantity of hydro-monobenzoporphyrin photosensitizer liposome formulations to be administered depends on the choice of active ingredients, the conditions to be treated, the mode of administration, the individual subject, and the judgement of the practitioner. Generally speaking, however, dosages in the range of 0.05-10 mg/kg may be needed. The foregoing range is, of course, merely suggestive, as the number of variables in regard to an individual treatment regime is large. Therefore,

. considerable excursions from these recommended values are expected.

Detailed Description Text (80):

For diagnosis, the hydro-monobenzoporphyrin photosensitizer compounds incorporated into liposomes may be used along with, or may be labeled with, a radioisotope or other detecting means. If this is the case, the detection means depends on the nature of the label. Scintigraphic labels such as technetium or indium can be detected using ex vivo scanners. Specific fluorescent labels can also be used but, like detection based on fluorescence of the photosensitizers themselves, these labels can require prior irradiation.

Detailed Description Text (82):

The methods of preparing the liposomal compositions of the present invention, the compositions themselves, and the method of using them in photodynamic treatment are described in greater detail in the examples below. These examples are readily adapted to the production and use of analogously described liposomes by simple substitutions of appropriate hydro-monobenzoporphyrin photosensitizers, additional phospholipids or alternative methods. The following examples are being presented to describe the preferred embodiments, utilities and attributes of the present invention, but they not meant to limit the invention. For example, although BPD-MA is used as the hydro-monobenzoporphyrin photosensitizer to form liposomes, the invention is not intended to be limited to this particular photosensitizer.

Detailed Description Text (85):

Three 100-ml batches of BPD-MA liposomes were prepared at room temperature (about 20.degree. C.), using the following general procedure. BPD-MA, butylated hydroxytoluene ("BHT"), ascorbyl palmitate, and the phospholipids DMPC and EPG were dissolved in methylene chloride, and the resulting solution was filtered through a 0.22 .mu.m filter. The solution was then dried under vacuum using a rotary evaporator until the amount of methylene chloride in the solid residue was not detectable by gas chromatography.

Detailed Description Text (88):

The filterability of these three batches was tested according to the following method: After the liposome composition had been passed three times through a Microfluidize.TM., a sample was withdrawn with a syringe. The volume of the sample withdrawn depended on a visual estimation of the filterability of the composition. The syringe was connected to a 0.22 .mu.m hydrophilic filter and was then placed in a syringe pump. The rate of piston movement was set at 10 ml/min, and filtrate was collected until the filter became blocked by large liposome aggregates. The volume of the filtrate was measured and recorded as ml/cm.sup.2. The results are summarized below in Table 2.

Detailed Description Text (90):

According to the slope of this equation, for every one-gram increase in DMPC or EPG lipid present, a 23-fold improvement in the filterability of the liposome formulation was achieved. The plot further indicates that, if the total lipid concentration became less than 1.52% with a BPD-MA photosensitizer concentration of 2.1 mg/ml, the liposome composition would not be capable of filtration through a 0.22 .mu.m filter at all.

Detailed Description Text (93):

A larger batch of BPD-MA liposomes (1.2 liters, i.e., 12 times the 100-ml batches of Example 1) was prepared using the molar ratio 1:3:5 (photosensitizer:EPG:DMPC) at room temperature (about 20.degree. C.). The contents of composition is described below in Table 3:

Detailed Description Text (95):

The slight increase in lipid content greatly increased the filterability of the liposome composition. Moreover, the yield was nearly 100%, with a 99.5% (by HPLC analysis) photosensitizer potency being maintained after sterile filtration.

Detailed Description Text (98):

Four batches of BPD-MA liposome compositions, each having the same photosensitizer/DMPC-EPG lipid molar ratio (1.05:3:5), were prepared using different

- film hydration temperatures. Data for these four batches, presented below in Table 5, were compared to demonstrate the relationship of potency loss and film hydration temperature.

Detailed Description Text (102):

A pair of 0.53-liter batches (photosensitizer:EPG:DMPC=1.05:3:5) was used to study the relationship between filterability and homogenization temperature. The compositions were prepared as described above in Example 1 using a hydration temperature of 45.degree. C. and a Microfluidizer.TM. with the outlet temperature set at 35.degree. C. The data showed that, at high hydration and homogenization temperatures, the relative filterability of BPD-MA liposome compositions increased after the initial passes through a Microfluidizer.TM. (#1 to #2), as expected, but then decreased for additional passes (#2 to #4), as seen below:

Detailed Description Text (104):

The data show that the filterability increased from passes #3 to #5, as expected, but then dropped back to the original value in passes #6 to #9. In contrast, the average particle size of the liposomes in the composition was reduced from 710 nm at pass #1 to as small as 247 nm at pass #6. However, as additional passes were made, the particle size unexpectedly increased to about 300 nm.

Detailed Description Text (106):

Preparation of Liposomes of the Invention

Detailed Description Text (107):

A 100-ml batch of BPD-MA liposomes is prepared at room temperature (about 20.degree. C.) using the following general procedure. BPD-MA, butylated hydroxytoluene ("BHT"), ascorbyl palmitate, and the phospholipids DMPC and EPG are dissolved in methylene chloride. The molar ratio of photosensitizer:EPG:DMPC is 1.0:3:7 and has the following composition:

Detailed Description Text (110):

The filterability of the batch is tested by the following procedure: After the liposome composition has been passed three times through a Microfluidizer.TM., a sample is withdrawn with a syringe. The volume of the sample withdrawn is about 20 ml, depending on a visual estimation of the filterability of the composition and assessment of the quality of the liposomes. The syringe is connected to a 0.22 .mu.m hydrophilic filter and is then placed in a syringe pump. The rate of piston movement is set at 10 ml/min, and filtrate is collected until the filter becomes blocked by large liposome aggregates. The filtrate is measured and recorded as ml/cm.sup.2 or g/cm.sup.2.

Other Reference Publication (6):

Jori et al., "Preferential delivery of liposome-incorporated porphyrins to neoplastic cells in tumour-bearing rats," Br. J. Cancer, 48:307-309 (1983).

Other Reference Publication (9):

Ricchelli, "Liposomes as carriers of hydrophobic photosensitizers in vivo: increased selectivity of tumor targeting," New Directions in Photodynamics Therapy, 847:101-106 (1987).

CLAIMS:

1. A method for making a pharmaceutical composition containing liposomes, said liposomes comprising a therapeutically acceptable amount of a hydro-monobenzoporphyrin photosensitizer and a mixture of phospholipids comprising egg phosphatidyl glycerol ("EPG") and dimyristoyl phosphatidyl choline ("DMPC"), wherein said method comprises the steps of:

- a. combining the photosensitizer and the phospholipids in a molar ratio of 1:7.0 or more phospholipid in the presence of an organic solvent;
- b. removing said organic solvent to form a photosensitizer:phospholipid complex;
- c. hydrating said photosensitizer:phospholipid complex with an aqueous solution at a

temperature below the glass transition temperature of the photosensitizer:phospholipid complex to form coarse liposomes containing said photosensitizer-phospholipid complex; and

d. homogenizing or reducing the particle size of said coarse liposomes to a particle size range of below about 300 nm at a temperature below the glass transition temperature of the photosensitizer:phospholipid complex.

17. A pharmaceutical composition containing liposomes in the particle size range of about 150 to 300 nm, wherein said liposomes comprise:

a. a therapeutically acceptable amount of a photosensitizer and

b. a mixture of phospholipids comprising:

(1) egg phosphatidyl glycerol ("EPG") and

(2) dimyristoyl phosphatidyl choline ("DMPC"),

wherein the molar ratio of said photosensitizer and said mixture of phospholipids is about 1:7.0 or more phospholipid.